Polymorphism – Multiple alternative forms of a gene or protein. Occurs naturally in population.
Polysome – An mRNA associated with a series of ribosomes involved in translation.
Primer – Short oligonucleotide which binds to specific single-stranded target nucleic acid sequence enabling polymerase to initiate strand synthesis.
Probe – A short, specific DNA sequence labelled with ^{32}P or biotin which can be used to detect complementary sequences on blots, etc.
Promoter – A DNA sequence that binds with RNA polymerase to initiate transcription.
Promoter/enhancer sequence – DNA sequence that is a control point for gene transcription. Promoter sequences are usually in the vicinity of the 1st exon; enhancer sequences may be many Kb upstream or downstream of the gene.
Proofreading ability – The ability of a polymerase enzyme to detect and correct mistakes that have been made in DNA synthesis.
Protein kinase – Family of enzymes catalyzing the transfer of a high energy phosphate from ATP to specific residues on proteins (often tyrosine, but also serine/threonine); one of the major mechanisms for regulation of protein function.
Proto-oncogene – A cellular gene whose alteration has been shown to be involved in malignant transformation.
Pro-virus – A viral genome integrated into a host cell genome.

Adverse drug reaction of the month

Hepatitis B vaccine and neurotoxicity

Munir Pirmohamed, Peter Winstanley

The availability of an effective vaccine against hepatitis B in recent years represents a major breakthrough in the prevention of a serious and occasionally fatal infection. In the UK, immunisation against hepatitis B is recommended for high-risk groups including healthcare workers. However, in certain cases, vaccination can lead to serious and unexpected adverse reactions. We describe the case of a male patient who developed cranial nerve palsies following hepatitis B vaccination.

Adverse drug reaction report

A 35-year-old previously fit and healthy male healthcare worker was admitted with a two-day history of progressively worsening vertigo, and a one-day history of nausea and inability to close his left eye. He also complained of tinnitus but not of deafness. All these symptoms had been preceded by an upper respiratory tract viral infection for five days. The patient was not on medication; however, four days before admission, he had received a booster dose of recombinant hepatitis B vaccine (Engerix B®). On examination, the patient had a left lower motor neuron facial nerve palsy and second degree nystagmus with the fast phase towards the right side, both of which suggested a left pontine lesion. There were no cerebellar signs or any other abnormal neurological signs. The erythrocyte sedimentation rate was normal. Magnetic resonance imaging (MRI) of the brain on admission did not show evidence of demyelination. The lumbar puncture was normal, and in particular, there was no oligoclonal IgG. Visual evoked responses were also normal. All viral titres were non-significant.

Within 24 h of admission, the patient's vestibular symptoms began improving, and had completely resolved by five days. The facial nerve palsy took two months to resolve completely. A repeat MRI scan performed three months after the initial presentation failed to show any evidence of a structural abnormality within the brain.

Discussion

The two main diagnoses considered in the patient were a first episode of multiple sclero-

Suspected adverse drug reactions reported with hepatitis B vaccination

Neurological
- relapse of multiple sclerosis
- Guillain-Barre syndrome
- polyneuropathy
- transverse myelitis
- facial nerve palsy
- cerebellar ataxia
- visual loss
- uveitis

Cutaneous
- angioedema
- erythema nodosum
- erythema multiforme
- urticaria
- lichen planus
- systemic lupus erythematosus

Miscellaneous
- acute glomerulonephritis
- polyarthritis

Box 1

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sis, and an adverse reaction to the hepatitis B vaccine. The former was thought to be unlikely given the the normal MRI scans, lumbar puncture and visual evoked responses. The temporal relationship between administration of the hepatitis B vaccine and onset of symptoms favours the latter diagnosis. Indeed, there is evidence that hepatitis B vaccination may lead to a variety of serious adverse events (box 1).[1] For example, it may precipitate multiple sclerosis in genetically predisposed individuals,[2] although a causal relationshop has not been definitely established. Additionally, facial paralysis[3] (as in this patient), acute cerebellar ataxia[4] and Guillain-Barre syndrome[5] have also been reported. On the Committee on Safety of Medicines/Medicines Control Agency database, there have been three reports of facial palsy, six of Guillain-Barre syndrome and nine of multiple sclerosis.

To the best of our knowledge, this is the first reported case of the involvement of both the seventh and eighth cranial nerves after hepatitis B vaccination. An immune pathogenesis secondary to molecular mimicry seems the most likely explanation for the occurrence of these adverse effects.[1] Although a causal association cannot be proved on the basis of this report, the clinical features and previous reports of neurological dysfunction would all support that this was an uncommon adverse reaction to the hepatitis B vaccine. The risk of neurotoxicity after hepatitis B vaccination is unknown and requires further study. However, these reactions are uncommon, and certainly the risk is not as high as that of contracting hepatitis B after needlestick injury from an infected patient (estimated to be about 10%). Thus, the risk–benefit ratio still favours vaccination of groups at high risk of exposure to hepatitis B.

Learning points

- it is often difficult to distinguish between disease and drug-induced toxicity. It is important to obtain a drug history from all patients: this should include not only prescribed medications, but also vaccinations and over-the-counter medications
- definite proof that a drug is responsible for the patient's symptoms is often not available. However, causality can be inferred from several points including the temporal relationship between the start of drug and onset of symptoms, whether symptoms resolve on drug withdrawal, any history of rechallenge, any previous reports of similar side-effects and biological plausibility
- hepatitis B vaccination can occasionally lead to a variety of serious adverse reactions which can affect many different organ systems including the central nervous system. These reactions are thought to be immune-mediated
- doctors should be aware that such serious adverse reactions may occasionally occur after vaccination for hepatitis B, although it is important to note that the benefit of this vaccine still outweighs the risks

Box 2

1 Dittmann S. Immunobiological preparations. In: Aronson JK, van Boxtel CJ, eds. *Side effects of drugs annual 18*. Amsterdam: Elsevier, 1995; pp 325–41.
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3 Ganry O, Lerailler F, Vercelletto M, Chiffoleau A, Larousse C. Peripheral facial paralysis following immunisation for hepatitis B: a case report. *Therapie* 1992; **47:** 437–8.
4 Deisenhammer F, Pohl P, Bosch S, Schmidauer C. Acute cerebellar ataxia after immunisation with recombinant hepatitis B vaccine. *Acta Neurol Scand* 1994; **89:** 462–3.
5 Tuohy PG. Guillain-Barre syndrome following immunisation with synthetic hepatitis B vaccine. *NZ Med J* 1989; **44:** 114–5.